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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/834,321	04/13/2001	Jeffrey V. Ravetch	TRU-0005	2584

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EXAMINER	
BELYAVSKYI, MICHAIL A	
ART UNIT	**PAPER NUMBER**
1644	15

DATE MAILED: 04/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/834,321	RAVETCH, JEFFREY V.	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this c mmunication appears on the c ver sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *14 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *3,5-9 and 16-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4 and 10-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 February 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 2/14/03 (Paper No. 12), is acknowledged.

Claims 1-21 are pending.

Claims 3, 5-9 and 16-21 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

Claims 1-2, 4 and 10-15 , drawn to a method for enhancing cytotoxicity with an antibody, wherein the antibody are specific for a HER2/neu growth factor receptor or for CD20 B cell antigen are under consideration in the instant application.

In view of the amendment, filed 2/14/03 (Paper No. 12), the following rejections remain:

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-2, 4, and 10-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention essentially for the same reasons set forth in the previous Office Action, Paper No: 10, mailed 10/22/02.

Applicant's arguments, filed 2/14/03 (Paper No. 12), have been fully considered, but have not been found convincing.

Applicant asserts that the claims under consideration do not require the use of antibodies. Applicant further asserts that to practice claimed inventions several alternative methods can be used. For example, methods including the use of antisense molecule, the use of synthetic oligonucleotides and the use of intracellular antibodies which inhibit expression or function of the proteins involved.

Applicant is respectfully reminded that because each alternative method represent a patentably distinct invention the restriction requirement was set forth for each method as separate group in Paper NO:7, mailed 3/07/02.

Applicant elected Group II, drawn to a method for enhancing cytotoxicity with an antibody, wherein the antibody are specific for a HER2/neu growth factor receptor or for CD20 B cell antigen.

Applicant has received an action on the merits for the elected claims of Group II. These claims require the use of antibodies that have a reduced binding affinity for FcRIIB , due to modification of the Fc portion of the antibody , while retaining or enhancing binding to FcRIIA and Fc RIIIA and use them in a method for enhancing cytotoxicity elicited by a this antibody *in vivo*, which method comprises disrupting activation of SHIP by Fc RIIB .

Applicant acknowledge that to practice the invention it would be essential that antibodies, while reducing their binding affinity for FcRIIB , due to modification of the Fc portion of the antibody , still retaining or enhancing binding to FcRIIA and FcRIIIA (page 7, lines 10-15 of specification as filed). However, the specification does not provide sufficient guidance and examples as to which modifications would be acceptable to retain these specific structural and functional properties of claimed antibodies to be used in the claimed method for enhancing cytotoxicity elicited by antibody *in vivo,* which method comprises disrupting activation of SHIP by FcRIIB In addition, the term "modifying" encompass any substitution, deletion or insertion (page 14, lines 13-16 of Specification as filed) of Fc portion of the antibody that will affect their structural and functional properties.

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed method for enhancing cytotoxicity elicited by a therapeutic antibody *in vivo*, which method comprises disrupting activation of SHIP by Fc RIIB in manner reasonably correlated with the scope of the claims. *In re Fisher*, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, lack of working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

4. Claims 1-2, 4, and 10-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention essentially for the same reasons set forth in the previous Office Action, Paper No: 10, mailed 10/22/02.

Applicant's arguments, filed 2/14/03 (Paper No. 12), have been fully considered, but have not been found convincing.

Applicant asserts that modified antibody do not require to practice claimed methods. In addition Applicant asserts that the specification describes the modified antibodies sufficiently so as to satisfy the requirements 35 U.S.C. 112 first parapraph.

Contrary to applicant assertion, as has been discussed supra, it is the Examiner position that the elected claims of Group II do require modified antibody to practice claimed method.

The claims as written encompass the genus of antibodies that have a reduced binding affinity for FcRIIB , due to modification of the Fc portion of the antibody , while retaining or enhancing binding to FcRIIA and Fc RIIIA that can be used in a method for enhancing cytotoxicity elicited by a this antibody *in vivo*, which method comprises disrupting activation of SHIP by Fc RIIB .

However, there does not appear to be an adequate written description in the specification as-filed how to make an antibody that have a reduced binding affinity for FcRIIB , due to modification of the Fc portion of the antibody , while retaining or enhancing binding to FcRIIA and Fc RIIIA and use them in a method for enhancing cytotoxicity elicited by antibody *in vivo,* which method comprises disrupting activation of SH2 domain containing inositol 5-phosphatase (SHIP) by FcRIIB .

The Examiner notes that the claimed invention which is drawn to a genus may be adequately described if there is a (1) sufficient description of a representative number of species, or (2) by disclosure of relevant, identifying characteristics sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention. To satisfy the disclosure of a "representative number of species" will depend on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. "Relevant, identifying characteristics" include structure or other physical and /or chemical properties, functional characteristics coupled with a known or disclosed correlation between function and structure, or a combination of such identifying characteristics sufficient to show the applicant was in possession of the claimed genus. (see Revised Guidelines for the Examination of Patent Applications Under the 35 U.S.C.112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No.4, pages 1099-1111, Friday January 5, 2001).

In the instant case, however, there is no described or art-recognized correlation or relationship between the structure of the invention, modified antibody, that reduced binding affinity for FcRIIB , due to modification of the Fc portion of the antibody , while retaining or enhancing binding to FcRIIA and Fc RIIIA that can be used in a method for enhancing cytotoxicity elicited by a this antibody *in vivo*, which method comprises disrupting activation of SHIP by Fc RIIB, the feature deemed essential to the instant invention. Therefore, one of skill in the art would not envisage, based on the instant disclosure, the claimed method for enhancing cytotoxicity with an antibody, wherein the antibody are specific for a HER2/neu growth factor receptor or for CD20 B cell antigen.

5. No claim allowed

6. **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is (703) 308-4232. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Michail Belyavskyi, Ph.D.
Patent Examiner
Technology Center 1600
April 7, 2003

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
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